Deliberative Scenario: Return of Genetic Research Results

In the 1940s, researchers recruited over 5,000 people from the town of Framingham, Massachusetts to participate in a study to discover the causes of heart disease. Over 60 years later, the children and grandchildren of the original cohort are also enrolled in the study, in addition to new cohorts with diverse racial and ethnic backgrounds.[1]

The Framingham Heart Study is one of the largest and longest running research projects in the United States. Over the life of the study, researchers have added new objectives and new tools and tests in response to advancing science and technology, which have given rise to new ethical considerations. One new objective is to discover associations between genetic mutations and disease, leading researchers to begin conducting genetic testing. This fictionalized deliberative scenario is loosely based on an ethical issue encountered by the study.

You are a member of the study's ethics board. The investigators have decided to embark on genetic research to better understand the *genetic* risk factors for certain diseases. It has always been common practice in the study to inform participants about concerning results, but genetic information can be different—it can reveal a wider array of information than other tests, the meaning of which can be uncertain. In addition, it can reveal information about biological relatives, who have not consented to be in the study, and put participants in the position of having to decide whether to disclose genetic information to them. Many of the participants are likely to have one or several genetic mutations—some of which might lead to cancer, others of which have unknown effects.

As a member of the ethics board, you are tasked with recommending policies for dealing with the results of these genetic tests, based on the information in the fictional memo below.

[1] Framingham Heart Study. (n.d.). History of the Framingham Heart Study. Retrieved August 29, 2016 from https://www.framinghamheartstudy.org/about-fhs/history.php

To: Members of the Ethics Committee
From: Heart Study Investigators
Re: Genetic research results

As you know, the Heart Study will undertake large-scale genomic analyses with our thousands of participants. A research objective is to discover associations between genetic mutations and disease outcomes. Given the large number of research participants and the volume of associated clinical and demographic data, this is likely to make a substantial

contribution. In the course of this research, however, we estimate that we will discover that many of our participants will have other mutations unrelated to the outcomes we are studying. The question before you is whether and how we should disclose those results.

It is currently our policy to disclose clinically significant findings to participants even if they are findings we were not looking for. For example, our researchers disclose high blood pressure results as soon as they are discovered, and they conduct follow-up calls with our participants after other test results come in to notify them of any possibly concerning results, such as abnormal cholesterol levels or blood panel abnormalities.

Genetic information, however, presents different issues. Whereas high cholesterol is a clinically significant result that is easily followed-up by our participants' regular health care providers, genetic results might be harder to interpret. There is no guarantee that our participants' primary care providers will have sufficient understanding of the meaning of those genetic results to give our participants appropriate guidance. In addition, even with sufficient understanding, the clinical significance of mutations might be unclear or unknown. For example there is still debate in the scientific community over the percentage of increased risk for breast cancer associated with the BRCA mutations, and the correct way to intervene when a BRCA mutation is discovered.

Patients' perceptions and understandings of risk can play a role in how they react to news about a genetic mutation, how

they interpret their clinician's advice, and what course of action they decide to take.

We are not equipped with the staff or resources to provide genetic counseling to our participants to help deliver the news. Even analyzing all of these genetic results (that are not part of our study) and contacting each participant to notify them would strain resources and be logistically difficult.

There are also other issues to consider. The validity of some of the findings is unclear and there is potential for participants to seek dramatic follow-up care or procedures based on questionable validity. Some of these follow up procedures have the potential to deeply affect individuals' lives and might be unnecessary. In addition, genetic tests provide information about the individual tested as well as their blood relatives. In our case, we could discover information about someone who is not enrolled in our study and did not consent to genetic testing. What are our obligations, if any, to family members?

On the other hand, disclosing this genetic information to our participants could save their lives in certain circumstances. Discovering an increased risk for cancer, for example, affords an individual the opportunity to speak with their primary care provider about additional screening, careful monitoring, and potential preventive measures. Discovering that an individual is a carrier for a particular disease allows them to make more informed reproductive choices, potentially opting for clinical testing of themselves, their partners, and potentially their fetuses or children. In addition, although receiving bad news

about a genetic predisposition for an incurable disease can be psychologically challenging, it also contributes to an individual's autonomy, helping them make more informed decisions about their lives — including financial and reproductive decisions, among others.

We are in a unique position to discover and disclose this information to our participants. Many of them likely will not access their genetic information for another reason. We are looking for guidance on both whether and *how* to disclose genetic findings to our participants.

To address this problem comprehensively, you have broadened the members of the ethics committee to include institutional review board members, researchers, research participants, lawyers, study administrators, and other stakeholders relevant to the decision making process.

Please come to the deliberation having read the following pieces of background information:

- "Guide to Classroom Deliberation for Students and Teachers"
- Fabsitz, R.R., et al. (2010). Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants. *Circulation: Cardiovascular Genetics*, 3, 574-580, Available at: http://circgenetics.ahajournals.org/content/3/6/574.full. (Introduction, Methods, and Charge to the Working Group)
- Presidential Commission for the Study of Bioethical Issues (PCSBI). (2013, December). Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts. Washington, DC: PCSBI, pp. 1-20. Available at: http://bioethics.gov/sites/default/files/FINALAnticipateCommunicate_PCSBI_0.pdf.